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101

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/508,418	06/08/00	HORIKOSHI	M 058140
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HM12/0821

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EXAMINER
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STEADMAN, D.	
ART UNIT	PAPER NUMBER

1652  
DATE MAILED:

13

08/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

**Office Action Summary**

<b>Application No.</b> 09/508,418	<b>Applicant(s)</b> HORIKOSHI ET AL.	
<b>Examiner</b> David J. Steadman	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1)  Responsive to communication(s) filed on \_\_\_\_\_.
- 2a)  This action is FINAL.
- 2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4)  Claim(s) 1-26 is/are pending in the application.
  - 4a) Of the above claim(s) 9-26 is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) 1-8 is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All b)  Some \* c)  None of:
    - 1.  Certified copies of the priority documents have been received.
    - 2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    - 3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  - \* See the attached detailed Office action for a list of the certified copies not received.
- 14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a)  The translation of the foreign language provisional application has been received.
- 15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5)  Notice of Informal Patent Application (PTO-152)
- 6)  Other:

## DETAILED ACTION

### *Status of the Application*

Claims 1-26 are pending.

Applicants election without traverse of Group I, claims 1-8, drawn to a protoporphyrinogen oxidase polypeptide in Paper No. 7, filed 04/11/01 is acknowledged.

Claims 9-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

It is noted that an Information Disclosure Statement (Form PTO-1449) has been submitted with the instant application. However, five (5) of the cited references are not present in the application and therefore, cannot be considered as per Applicants request. The Examiner invites Applicants to submit additional copies of the **non-initialed** references indicated on Form PTO-1449 and upon receipt, will consider the references and return Form PTO-1449 in a subsequent communication.

### *Drawings*

1. The drawings submitted with this application were objected to by the Draftsperson. Please see attached Form PTO-948 for comments. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

### *Specification/Informalities*

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Art Unit: 1652

The following title is suggested: "Herbicide-Resistant Protoporphyrinogen Oxidase Isolated From *Nicotiana tabacum*".

### *Claim Objections*

3. Claims 6-8 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). In the interest of compact prosecution, the claims have been examined on the merits.

4. Claims 3 and 4 are objected to because of the following informalities: the term "polypeptide have an enzyme activity" is grammatically incorrect and should be replaced with, for example, "polypeptide has an enzyme activity". Appropriate correction is required.

5. Claims 1-5 are objected to because of the following informalities: the term "SEQ ID No.2" uses an improper format to denote a sequence and should be replaced with, for example, "SEQ ID NO:2". Appropriate correction is required.

### *Claim Rejections - 35 USC § 101*

6. Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a protoporphyrinogen polypeptide of SEQ ID NO:2 or variants thereof. The claims read on a product of nature and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

### *Claim Rejections - 35 USC § 112*

Art Unit: 1652

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
8. Claims 1-4 (claims 6-8 dependent thereon) are unclear in the recitation of “substantially equivalent”. It is suggested that, for example, the term “substantially” be deleted.
9. Claims 2-5 (claims 6-8 dependent thereon) recite the limitation “the protophyrinogen oxidase”. There is insufficient antecedent basis for this limitation in the claims.
10. Claims 3 and 4 are indefinite in the recitation of the term “a transit peptide is deleted” as it is unclear as to the amino acids of the polypeptide of SEQ ID NO:2 that compose said transit peptide. It is suggested that Applicants identify the transit peptide by specific numbering of amino acids of SEQ ID NO:2.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 3, 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Art Unit: 1652

Claims 1, 3 (claims 6-8 dependent thereon) are directed to a genus of protoporphyrinogen oxidase (protox) polypeptides as encompassed by the claims. The specification teaches the structures of only two representative species of such polypeptides, i.e., SEQ ID NOs:2 and 11. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a protox polypeptide tolerant to photobleaching herbicide. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

12. Claims 1, 3, 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protox polypeptide of SEQ ID NO:2 that is resistant to Compounds A-E set forth in the specification at page 6, does not reasonably provide enablement for any protox polypeptide or any protox polypeptide with a deleted transit peptide tolerant to any photobleaching herbicide, derivative thereof, or pyrazole compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 3, (claims 7, 8 dependent thereon), 6 are so broad as to encompass any protox polypeptide or any protox polypeptide with a deleted transit peptide tolerant to any photobleaching herbicide, derivative thereof, or pyrazole compound. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of protox polypeptides and photobleaching herbicides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional

Art Unit: 1652

properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the protox polypeptide of SEQ ID NO:2 that is resistant to Compounds A-E set forth in the specification at page 6.

While enzyme isolation techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any protox polypeptide or any protox polypeptide with a deleted transit peptide tolerant to any photobleaching herbicide, derivative thereof, or pyrazole compound because the specification does not establish: (A) regions of the polypeptide structure which may be modified by addition, deletion, substitution, or insertion without affecting protox activity and without further affecting the tolerance to any photobleaching herbicide, derivative thereof, or pyrazole compound; (B) the general tolerance of protox to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any protox residues with an expectation of obtaining protox

Art Unit: 1652

activity and further obtaining resistance to any photobleaching herbicide, derivative thereof, or pyrazole compound; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any protox polypeptide or any protox polypeptide with a deleted transit peptide tolerant to any photobleaching herbicide, derivative thereof, or pyrazole compound. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

13. Claims 1, 3, 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ward et al. (WO95/34659). Claims 1, 3, 6-8 are drawn to the protox polypeptide of SEQ ID NO:2 and



Art Unit: 1652

deletion, substitution, and addition mutants thereof as encompassed by the claims. Ward et al. teach mutant *Arabidopsis thaliana* and *Zea mays* protox polypeptides that are resistant to pyrazole-based herbicides. This anticipates claims 1, 3, 6-8 as written.

14. Claims 1, 3, 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Volrath et al. (US Patent 5,939,602). Claims 1, 3, 6 are drawn to the protox polypeptide of SEQ ID NO:2 and deletion, substitution, and addition mutants thereof as encompassed by the claims. Volrath et al. teach a protox polypeptide that is 74 % identical to SEQ ID NO:2 of the instant application and is resistant to pyrazole-based herbicides. This anticipates claims 1, 3, 6 as written.

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ward et al. in view of Lermontova et al. (Proc Natl Acad Sci 94:8895-8900). Claims 1-8 are drawn to the herbicide-resistant protox polypeptide of SEQ ID NO:2 and deletion, substitution, and/or addition mutants thereof as encompassed by the claims and optionally resistant to the compounds of claims 6-8.

Ward et al. teach an herbicide-resistant *A. thaliana* protox polypeptide with substitution of valine for alanine at amino acid 220 of *A. thaliana* protox (p 65). The *A. thaliana* protox mutation taught by Ward et al. results "in at least a 10-fold increase" in the herbicide resistance

Art Unit: 1652

of *A. thaliana* protox (p 65). Ward et al. teach that mutation of alanine to valine at position 166 of *Z. mays* (corresponding to position 220 of *A. thaliana* protox) also increases herbicide resistance by at least 10-fold (p 64). Ward et al. do not teach an herbicide-resistant *Nicotiana tabacum* protox polypeptide with a substitution of alanine with valine at amino acid 231, with or without a deleted transit peptide.

Lermontova et al. teach cloning and expression of wild-type, i.e., non-herbicide resistant, *N. tabacum* protox isoenzyme I (p 8895-96, Materials and Methods). The polypeptide of Lermontova et al. is 99.2 % identical to the polypeptide of SEQ ID NO:2 of the instant application. Lermontova et al. show an amino acid sequence alignment of wild-type *N. tabacum* protox isoenzyme I against wild-type *A. thaliana* protox (p 8897, Fig 1). Lermontova et al. teach that the *A. thaliana* protox shares a high similarity with *N. tabacum* protox isoenzyme I. The sequence alignment of the two enzymes shows *N. tabacum* protox isoenzyme I as having alanine at position 231, corresponding to position 220 of *A. thaliana* protox. Lermontova et al. further teach that yeast protox contains an N-terminal 13 amino acid signal peptide that directs the protein to the mitochondria and is visibly cleaved off and “A small transit peptide could be cleaved off from tobacco mitochondrial enzyme, although no clear-cut transit sequence is detectable” (p 8899, left column, bottom).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Ward et al. and Lermontova et al. for a mutant *N. tabacum* protox with alanine substituted with valine at position 231 with or without a deleted transit peptide. One would have been motivated to replace alanine with valine at position 231 of wild-type *N. tabacum* protox in order to create an herbicide-resistant *N. tabacum* protox. One would have been motivated to

Art Unit: 1652

cleave a transit peptide from *N. tabacum* protox in order to prevent translocation of the protox to the mitochondria. One would have a reasonable expectation of success for an herbicide-resistant *N. tabacum* protox with alanine substituted with valine at position 231 with or without a deleted transit peptide because of the results of Ward et al. and Lermontova et al. Therefore, claims 1-8, drawn to the herbicide-resistant protox polypeptide of SEQ ID NO:2 and deletion, substitution, and/or addition mutants thereof as encompassed by the claims and optionally resistant to the compounds of claims 6-8 would have been obvious to one of ordinary skill in the art.


### Conclusion

16. No claim is in condition for allowance.

Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4242. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

  
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